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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,002	CREGAN ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-19,21,22 and 24* is/are pending in the application.

4a) Of the above claim(s) *19,21,22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of June 26, 2009, to the non-final action dated February 26, 2009, has been entered. Claims 1, 4, 8, 10, 13-16 and 18 have been amended, and claims 2 and 7 cancelled. No claims were newly added. Accordingly, claims 1, 3-6, 8-19, 21, 22 and 24 remain pending in the application. Claims 19, 21, 22 and 24 stand withdrawn from further consideration, with traverse, as being drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. The claims have been examined commensurate with the scope of the elected invention. Claims 1, 3-6, 8-18 are under current examination.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on June 26, 2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner, and indicated as such on Applicants' IDS form.

Withdrawn Claim Objection

Claim 16(iii) was objected to for containing previously deleted text, in the previous Office action dated February 26, 2009. Applicants have amended the claim, rendering the objection moot. Thus, the objection is hereby withdrawn.

Withdrawn Claim Rejection - 35 USC § 112- New Matter

Claims 13 and 16 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement and introducing new matter, in the previous Office action dated February 26, 2009. Applicants have amended the claims to remove the new matter, obviating the grounds of rejection. Accordingly, the rejection is hereby withdrawn.

Withdrawn Claim Rejections - 35 USC § 112- Second Paragraph

Claims 1-6, 8, 11 and 13 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous Office action dated February 26, 2009. Applicants have amended base claim 1 to introduce essential steps; claim 8 has been amended to indicate that the cells are retained following washing, and claim 13 has been amended to clarify method steps. Thus, the rejections are hereby withdrawn.

Withdrawn Claim Rejection - 35 USC § 102

Claim 18 was rejected under 35 U.S.C. 102(b) as being anticipated by Stingl et al. (Breast Cancer Res. Treat. 67:93-109; 2001), in the previous Office action dated February 26, 2009. Applicants have amended the claim to read only on pluripotent progenitor cells. As the cells taught by Stingl et al. are bipotent mammary epithelial progenitor cells, the reference does not anticipate the claim. Thus, the rejection is hereby withdrawn.

Applicants' arguments are moot in view of the withdrawn rejection.

Withdrawn Claim Rejections - 35 USC § 103

Claims 1, 2 and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (Aus. J. Zool. 45:423-433; 1997), in view of Stingl et al. (Breast Cancer Res. Treat. 67:93-109; 2001); Claims 1, 3-5, 8, 12, 15 and 16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (Aus. J. Zool. 45:423-433; 1997), in view of Stingl et al. (Breast Cancer Res. Treat. 67:93-109; 2001), and further in view of Buehring, G. (J. Dairy Sci. 73:956-963; 1990); Claims 1, 7, 9, 10, 13 and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (Aus. J. Zool. 45:423-433; 1997), in view of Stingl et al. (Breast Cancer Res. Treat. 67:93-109; 2001), and Buehring, G. (J. Dairy Sci. 73:956-963; 1990), and further in view of Nghiem et al. (Methods 28:25-33; 2002); and Claims 1, 11 and 15-17 were rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (Aus. J. Zool. 45:423-433; 1997), in view of Stingl et al. (Breast Cancer Res. Treat. 67:93-109; 2001), and Buehring, G. (J. Dairy Sci. 73:956-963; 1990), and further in view of Goldman et al. (U.S. Patent

Application Publication No.: 2004/0029269; effective filing date May 7, 2002), in the previous Office action dated February 26, 2009. Applicants' cancellation of claims 2 and 7 renders their rejections moot.

Applicants have amended the claims to read only on pluripotent progenitor cells. As the cells taught by Stingl et al. are bipotent mammary epithelial progenitor cells, and none of the secondary references describe the isolation of multipotent cells from a human female mammary secretion, the rejections are hereby withdrawn.

Applicants' arguments are moot in view of the withdrawn rejections.

New Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1, 3-6 and 8-18 are newly rejected under 35 U.S.C.§112, first paragraph, because the specification, while being enabling for a method of isolating cells having stem cell-like characteristics of SSEA-4 and Tra-1-60 marker expression, from human milk, and cells isolated by said method, does not reasonably provide an enablement for a method of isolating pluripotent progenitor cells from any human mammary secretions of a male or female, or pluripotent progenitor cells isolated from any human mammary secretion, as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is based on issues related to the absence of an enabling disclosure for the ability to isolate cells from any human mammary secretion that are pluripotent and can thus differentiate into any cells of the human body. In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Factors to be considered in determining whether a disclosure meets the enablement requirement

of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404:

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

MPEP § 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection."

The claims broadly encompass a method of isolating pluripotent progenitor cells from any human mammary secretions of a male or female, and pluripotent progenitor cells isolated from any human mammary secretion.

The Rule 1.132 Declaration by co-inventor Mark Cregan provides definitions of pluripotency that include: " Pluripotent stem cells can give rise to any type of cell in the body except those needed to develop a fetus"; "pluripotent cells are generally defined as stem cells, which are derived from totipotent stem cells and have the ability to differentiate into any cell type of an organism, and can develop into various cells, tissues, or organs (except the cells of the placenta or other supporting tissues of the uterus)"; and with reference to the instant specification: "pluripotent cells are defined as embryonic stern cells which are capable of generating into all differentiated cells types within the body". Thus, Applicants' own definitions require that pluripotent cells be able to differentiate at least into the cells of the three germ layers or lineages (ecotoderm, endoderm and mesoderm).

The instant specification describes the isolation of cells from human hind milk (breastmilk) by centrifugation, followed by cell culture on Matrigel™ coated plates (pages 14-15 and Figure 8), or by isolation from human milk using extracellular markers Tra-1-60 and SSEA-4 bound to magnetic beads, followed by cell culture (page 13 and Figures 2, 5 and 6).

The specification is silent however, on the differentiation of the cells into any other cell type or lineage. Applicants' disclosure on page 15, with regard to primary culture of the cells on Matrigel™ coated plates, states: "That the cells appear undifferentiated and many can be

observed to have a large nucleus to cytoplasm ratio is even more evidence for a progenitor like identity". The specification states in the brief description of Figure 5, that after several months in culture, these cells do not appear to have differentiated into other cell types; and in the brief description of Figure 6, that after 2 months in culture the stem cells have not differentiated (page 7); leaving the skilled artisan to carry out further experimentation to test whether such "progenitor-like" cells would be capable of differentiating into any other type of cells. Moreover, the outcome of such experimentation for differentiation into the numerous types of cells, as claimed would be unpredictable, constituting an undue burden on the skilled artisan.

Thus, the disclosure is merely an invitation to a person of skill in the art to engage in further experimentation to discover whether the Tra-1-60 and SSEA-4 positive cells isolated from human milk are capable of differentiating into any of numerous cell types, as claimed, and whether such cells may be isolated from any type of mammary secretion from a male or female. Please note "case law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves." *In re Gardner* 166 USPQ 138 (CCPA) 1970.

The Federal Circuit has stated that: a specification need not disclose what is well known in the art. See, e.g., *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. *Genentech Inc. v. Novo Nordisk A/S,* 42 USPQ2d 1005 (CAFC 1997).

The prior art at the time of filing did not teach the any pluripotent stem cells isolated from human mammary secretion, as instantly claimed. The prior art is further silent on the differentiation of any cells from human mammary secretion into cells of the three germ layers. +

It should be noted that the presence of Tra-1-60 and SSEA-4 markers on the surface of a cell is not sufficient to show pluripotency of the cell. The prior art of Badcock et al. (Cancer Res. 59:4715-4719; 1999), states that TRA-1-60 antigen is expressed by human PGC as well as carcinoma in situ cells and seminoma cells (second column, p. 4718). Additionally, Pera et al. (U.S. Patent Application Publication No.: 2005/0095708; Nov. 11, 2002), in describing the characterization and isolation of human ES (embryonic stem) cells, state: "The range of markers available to identify HES cells is large and may include determining the presence of any of the following cell markers for a positive identification. Suitable markers for distinguishing ES cells include SSEA-3, SSEA-4, GCTM-2, GDF-3, Cripto (Cr-1 and CR-1) or GDF-3, and genesis. However, none are absolutely specific markers for pluripotent, differentiated or undifferentiated cells." (Paragraph [0005], p. 1).

The detail of the disclosure provided by Applicants, in view of the prior art, must encompass a wide knowledge, so that the person skilled in the art would be able to practice the invention as claimed by Applicants, without undue burden being imposed on such person of skill. This burden has not been met because it would require undue experimentation to demonstrate the ability to discover and induce differentiation of Tra-1-60 and SSEA-4 positive cells isolated from any human mammary secretion, into all cell types of the body.

The guidance provided by the specification amounts to an invitation for the skilled Artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely sets forth the isolation of SSEA-4 and Tra-1-60 expressing cells, from human milk. Thus, the differentiation of such cells into the various cell types envisioned is based on conjecture.

Therefore, in view of the art recognized high level of unpredictability regarding the pluripotency of a cell based on the presence of two cell surface markers, and the teachings of the prior art, together with the large quantity of research required to define these unpredictable variables, and the lack of guidance provided in the specification regarding the same, it is the position of the examiner that it would require undue experimentation for one of skill in the art to practice the scope of the invention as broadly claimed. Hence, absent a strong showing by

Applicants, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

New Claim Rejection - 35 USC § 102

Applicants' claim amendments have necessitated the following new ground of rejection.

Claim 18 is newly rejected under 35 U.S.C. 102(b) as being anticipated by Draper et al. (Curr. Opinion, Obstet. Gynecol. 14:309-315; 2002).

The rejection has been applied to the extent that the claim may be enabled for cells having stem cell-like characteristics that include the expression of cell surface markers SSEA-4 and Tra-1-60.

Claim 18 recites cells isolated from human mammary secretion, derived using the method of claim 1. Thus, the claim is a product by process claim. MPEP 2113 further states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Similarly the tissue source of a product is not relevant, if the product is the same. For example, a fibroblast from a human foot can be the same as that from a human arm.

Draper et al. teach human pluripotent stem cells capable of differentiating into all the cell types present in the adult body (Abstract). Additionally teaching hES cells that displayed immunoreactivity with TRA-1-60 and SSEA-4 (second column, p. 311). The examiner further maintains that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of factual evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips,* 28 USPQ 1302, 1303 (BPAI 1993), *In re Best,*

562, F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray,* 10 USPQ2d 1922, 1923 (BPAI 1989).

Therefore Draper et al. anticipate the instant invention as claimed.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633